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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,712	05/15/2006	Christian Hesslinger	27319U	6309

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EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,712	HESSLINGER ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 11-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 11-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's request for continued examination filed on May 4, 2009.

The Advisory Action mailed on May 29, 2009 has been withdrawn, and is replaced with this NON-FINAL office action.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Status of Claims

Amendment of claims 1, 4, 6, 11, and 14-15, is acknowledged.

Claims 1-7, and 11-15 are currently pending and are the subject of this office action.

Claims 1-7, and 11-15 are currently under examination.

Priority

The present application claims priority to International Application No. PCT/EP04/52725 filed 10/29/2004 and to foreign application No. EP20030024844 filed 10/31/2003.

Rejections and/or Objections and Response to Arguments

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated (Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment and/or New Rejections and/or Objections not Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112 (New Rejection Necessitated by Amendment)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-7, and 11-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7 and 11-15 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap

between the elements. See MPEP § 2172.01. The omitted elements are: the patient population to be treated. The rejected claims fail to provide a subject for the verb "administering", so the claims are indefinite insofar as they do not say to whom the combination is administered

For the purpose of this examination the claims are being interpreted as if BH4 were administered to patients with respiratory diseases in general or COPD in particular (patients in need thereof) depending on which claim is being examined.

Claim Rejections - 35 USC § 103 (New Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1-3 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takafumi et. al. (EP0908182, cited by Applicant).

Claims 1-3 and 6 recite a method for treating a respiratory disease (COPD in claims 2-3 and 6) in a patient consisting of administering a therapeutically effective amount of BH4 and a pharmaceutically acceptable carrier to a patient in need thereof.

For claim 1-3 and 6, Takafumi teaches a method to treat diseases associated with dysfunction of NOS (i.e. decrease in NO) with BH4 preparations (see paragraphs [0021] and [0022] on page 4). With regards to the disease associated with dysfunction of NOS, the EP document teaches that respiratory diseases such as asthma, chronic obstructive pulmonary diseases, pulmonary hypertension and ARDS are known to be associated with decreased NO production (paragraph 0002, lines 31-34 of page 2).

Takafumi further teaches that the pharmaceutical compositions further comprise a pharmaceutically acceptable carrier (see paragraphs [0038]-[0039] on page 8).

Takafumi et al. does not explicitly teach a method of treating COPD or respiratory diseases in a patient consisting of administering to a patient in need thereof a therapeutically effective amount of BH4.

However, at the time of the invention, it would have been *prima facie* obvious for a person of ordinary skill in the art to administer BH4 to a patient suffering from COPD in view of the teachings of Takafumi. One would have been motivated to do so because as taught by Takafumi BH4 preparations are useful for treating conditions related to a decrease in NO production, and further, it is well known in the art that COPD is associated with a decrease in NO production as taught by Takafumi. Thus, one would have a reasonable expectation of success that by administering BH4 to a patient suffering from COPD in view of the teachings of Takafumi, one would achieve a method of treating COPD, thus resulting in the practice of claims 1-3 and 6 with a reasonable expectation of success.

Claim 4 rejected under 35 U.S.C. 103(a) as being unpatentable over Takafumi et. al. (EP0908182, cited by Applicant) as applied to claims 1-3 and 6, evidenced by Troosters et. al. (CAS accession # 2004339338 corresponding to Revue des maladies respiratoires (2004) 21:319-327). Use as in view of.

Claim 4 recites a method or treating muscular dysfunction in a COPD patient consisting of administering a therapeutically effective amount of BH4 and a pharmaceutically acceptable carrier.

For claim 4 Takafumi teaches a method to treat diseases associated with dysfunction of NOS (i.e. decrease in NO) with BH4 preparations (see paragraphs [0021] and [0022] on page 4). Among the diseases associated with decreased NO production (i.e. dysfunction of NOS) the authors mention: respiratory diseases in general and COPD in particular (see paragraph [0002] on page 2, lines 30-34). Takafumi further teaches that the pharmaceutical compositions further comprise a pharmaceutically acceptable carrier (see paragraphs [0038]-[0039] on page 8).

Takafumi does not teach the treatment of muscular dysfunction in a COPD patient; however statistically some COPD patients will have muscular dysfunction as evidenced by Troosters. Troosters teaches that Patients with COPD frequently have muscular dysfunction (see abstract, lines 4 and 5). In other words: COPD patients with muscular dysfunction are a subpopulation of the patients with COPD. So even though Takafumi is silent regarding the treatment of muscular dysfunction in a COPD patient, the above statement does not appear to result in a manipulative difference in the method steps when compared with the prior art disclosure since the same compound (BH4) is administered to the same population (COPD patients which covers the subpopulation of COPD patients with muscular dysfunction). In other words: products of identical chemical composition cannot exert mutually exclusive properties when administered under the same circumstances. It is a general rule that merely discovering

and claiming a new benefit or property (i.e. treating muscular dysfunction in a COPD patient with BH4) of an old process (treating COPD with BH4) cannot render the process again patentable. *In re Woodruff*, 16USPQ2d 1934, 1936 (fed. Cir. 1990).

In other words, by practicing the method of Takafumi (i.e. treating COPD with BH4) one will be practicing the method of the instant claim 4 (i.e. treating muscular dysfunction in a COPD patient with BH4), since as evidenced by Troosters the population of "COPD patients with muscular dysfunction" is a subpopulation of the patients with COPD.

Claims 5, 7, 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takafumi et. al. (EP0908182, cited by Applicant) as applied to claims 1-3 and 6 above, and further in view of Juturu et. al. (US 2004/0097467, cited in prior office action) or Rabelnik et. al. (US 6,544,994, cited in prior Office Action).

Claim 5 further limits claim 1, wherein the method further comprises a compound selected from the group consisting of arginine, L-arginine hydrochloride, etc (see claim 5 for a full list).

Takafumi teaches all the limitations of claim 5, except for further using arginine or any of the other compounds listed in claim 5.

However, Juturu et. al. teach a method of treating COPD with arginine silicate inositol complex (a source of arginine, see claims 44 and 45 and paragraph [0042]).

Also, Rabelnik et. al. teach that arginine is the precursor of endogenous nitric oxide (NO) and as a consequence it increases the production of NO (see column 2,

lines 3-18), and since Takafumi teaches that an increase of endogenous NO can be beneficial for the treatment of COPD or any other respiratory disease it would have been obvious to treat COPD or any other respiratory disease with arginine.

At the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to treat COPD or any respiratory disease combining two compositions (BH4 and arginine) each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art (see MPEP 2144.06). *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). All this would result in the practice of claim 5 with a reasonable expectation of success.

Claim 7 further limits claim 6, wherein the method further comprises a compound selected from the group consisting of arginine, L-arginine hydrochloride, etc (see claim 7 for a full list).

Takafumi teaches all the limitations of claim 7, except for further using arginine or any of the other compounds listed in claim 7.

However, Juturu et. al. teach a method of treating COPD with arginine silicate inositol complex (a source of arginine, see claims 44 and 45 and paragraph [0042]).

Also, Rabelnik et. al. teach that arginine is the precursor of endogenous nitric oxide (NO) and as a consequence it increases the production of NO (see column 2, lines 3-18), and since Takafumi teaches that an increase of endogenous NO can be

beneficial for the treatment of COPD or any other respiratory disease it would have been obvious to treat COPD or any other respiratory disease with arginine.

At the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to treat COPD or any respiratory disease combining two compositions (BH4 and arginine) each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art (see MPEP 2144.06). *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). All this would result in the practice of claim 7 with a reasonable expectation of success.

Claim 11 further limits claim 1, wherein the method further comprises a compound selected from the group consisting of arginine, L-arginine hydrochloride, etc (see claim 11 for a full list). Claims 12-15 recite the same limitations as claim 11, wherein the respiratory disease is COPD.

Takafumi teaches all the limitations of claims 11-15, except for further using arginine or any of the other compounds listed in claims 11 and 15.

However, Juturu et. al. teach a method of treating COPD with arginine silicate inositol complex (a source of arginine, see claims 44 and 45 and paragraph [0042]).

Also, Rabelnik et. al. teach that arginine is the precursor of endogenous nitric oxide (NO) and as a consequence it increases the production of NO (see column 2, lines 3-18), and since Takafumi teaches that an increase of endogenous NO can be

beneficial for the treatment of COPD or any other respiratory disease it would have been obvious to treat COPD or any other respiratory disease with arginine.

At the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to treat COPD or any respiratory disease combining two compositions (BH4 and arginine) each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art (see MPEP 2144.06). *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). All this would result in the practice of claims 11-15 with a reasonable expectation of success.

Withdrawn Rejections and/or Objections

Claims rejected under 35 USC 112, first paragraph (written description).

Due to applicant's amendment of claims 1, 4, 6, 11, and 14-15, the written description rejection is now moot.

Rejection under 35 USC 112, first paragraph (written description) is withdrawn.

Claims rejected under 35 USC 103 (a)

Upon careful consideration the 103(a) rejection is withdrawn.

However, based on new prior art a new 103(a) rejection is applied (see above).

Conclusion

No claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1612
August 10, 2009

/Brandon J Fetterolf/

Examiner, Art Unit 1642